IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#16 JM 11/13/02

Attorney Docket No. 017227/0159

In re patent application of

Suzanne CORY *et al.*

Serial No. 09/508,832 Group Art Unit: 1642

Filed: July 10, 2000 Examiner: M. Yu

For: NOVEL THERAPEUTIC MOLECULES

PETITION TO THE GROUP DIRECTOR

Group Director
Art Unit 1600
Washington, D.C. 20231

Sir:

Applicants hereby petition the Group Director of Art Unit 1600 under 37 C.F.R. §1.181 for the examination of additional nucleotide sequences. Under 37 C.F.R. §1.181(f), this petition is being filed on a timely basis, within two months of the mailing date of the Office communication dated August 23, 2002.

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicants hereby petition for any needed extension of time.

Action Requested

In accordance with MPEP §1893.03(d) and Example 17 of Annex B Part 2 of the PCT Administrative Instructions contained in Appendix AI of the MPEP, applicants petition for the Group Director to overturn the Examiner's finding of a lack of unity of invention.

At the very least, applicants request rejoinder and examination of protein SEQ ID NO: 10, with its coding sequence, SEQ ID NO: 9. SEQ ID NO: 10 is recited in claims 10, 15, 17, 18, and 60, and SEQ ID NO: 9 is recited in claims 7, 9, and 16.

Furthermore, in accordance with MPEP §803.04 and the Commissioner's Notice on Examination of Patent Applications Containing Nucleotide Sequences, 1232 OG 242 (116),

applicants petition for the examination of up to nine additional polynucleotide sequences and the proteins for which they code.

Statement of Facts

1. The Examiner issued an Office Action dated December 14, 2001, alleging a lack of unity of invention and dividing the claims into Groups I – XXII. The examiner found no unity of invention between any of the claimed polynucleotides and the proteins for which they code. The finding of a lack of a technical feature in the art was based on citation to β tubulin, which the Examiner stated was "a derivative of a polynucleotide having one or more of the identifying characteristics of Bim." Office Action dated December 14, 2001, at p. 6. (Bim is the protein with corresponding polynucleotides of the present invention.)

2. Applicants responded by requesting with traverse, *inter alia*, examination of SEQ ID NO: 10, with its coding sequence, SEQ ID NO: 9, as recited in Groups V and X. In support of the argument that β tubulin is totally unrelated to Bim, applicants attached a clustal protein alignment, between Bim_{EL} of (SEQ ID NO: 10) and ß tubulin, indicating that only 40 of the 198 amino acids are identical, *i.e.* there is less than 20% identity, which generally is regarded as insubstantial. *See* Response dated July 16, 2002, at p. 2. Moreover, applicants amended claims 1 and 10 to recite that the characteristic of Bim is the ability to induce apoptosis, thereby further to distinguish these claims over prior art disclosure of beta tubulin.

3. The Examiner issued an Office Action dated August 23, 2002, holding the finding of a lack of unity of invention to be final while admitting that SEQ ID NO: 9 was free of the prior art. In support of this finding of lack of unity of invention, the Examiner cited Oltavi *et al.*, which disclosed Bax, a protein associated with apoptosis. See Office Action dated August 23, 2002, at pages 4 and 15.

4. In response to the Office Action dated August 23, 2002, applicants file this petition. Applicants also submit a protein alignment analysis that shows the Bax protein of Oltavi is not even within the first 1000 significant alignments of SEQ ID NO: 9.

Argument

Request for Withdrawal of Restriction Between SEQ ID NO: 9 and SEQ ID NO: 10

Under Example 17 of Annex B Part 2 of the PCT Administrative Instructions contained in Appendix AI of the MPEP, it is improper to restrict between a protein and an encoding polynucleotide. Accordingly, applicants request rejoinder and examination of claims 7, 9, and 16, which recite SEQ ID NO: 9 and claims 10, 15, 17, 18, and 60 which recite SEQ ID NO: 10. These sequences are covered by Groups V and X (Applicants note that in the Office Action dated December 14, 2001, SEQ ID NO: 7 is indicated incorrectly as the coding sequence for SEQ ID NO: 10. Applicants elected Group X with the understanding that it is the Group X that reads on SEQ ID NO: 9.)

Applicants contend that the Examiner's finding of lack of unity of invention is improper. The Examiner has stated that there is no unity of invention among the claims because of the lack of a technical feature that defines a contribution over the prior art. To refute the finding of the Examiner's, applicants attach hereto as Exhibit 1, a Blastp (protein) alignment analysis that was performed against the Genbank nr database at NCBI using the human Bim_{EL} sequence (SEQ ID NO: 6). This alignment demonstrates that the Bax molecule of the Oltvai reference does not appear in any of the first 1000 significant alignments.

In conclusion, applicants request, at the very least, examination of all claims reciting SEQ ID NOs: 9 and 10 together, in compliance with the rules of the PCT.

Request for Withdrawal of Restriction Between Groups V and Groups I-IV

The Examiner's restriction of Groups I-IV, dividing each polynucleotide into a separate invention, is in violation of MPEP §803.04, which states that "***normally*** ten (10) sequences constitute a reasonable number for examination purposes." This is true even if each nucleotide sequence is an independent and distinct invention under 35 USC §121. The Commissioner has decided *sua sponte* to waive the requirements of 37 CFR §1.141 *et seq.* and to permit the claiming of a reasonable number of nucleotide sequences in an application, thereby to "aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office." Automatically restricting every single polynucleotide into separate applications will unduly burden applicants in the field of

biotechnology, and is contrary to the letter and spirit of the Commissioner's *sua sponte* waiver of 37 CFR §1.141 *et seq*.

Groups I-V recite five polynucleotide sequences, and applicants request that all sequences be examined together because they can be examined without undue burden and they are related. Groups I-V respectively recited the polynucleotide sequences for murine Bim_S (SEQ ID NO: 1), Bim_L (SEQ ID NO: 3), Bim_{EL} (SEQ ID NO: 5) and human Bim_L (SEQ ID NO: 7), and Bim_{EL} (SEQ ID NO: 9).

At the very least, applicants request examination of the *human* Bim_{EL} (SEQ ID NO: 9) and Bim_L (SEQ ID NO: 7) nucleic acid sequences. Bim_{EL} and Bim_L are different isoforms of the Bim molecule, and are closely related because they have the same function and effect. Moreover, their structure is similar in that Bim_L is essentially a truncated version of Bim_{EL}

Applicants also request examination of murine Bim_S (SEQ ID NO: 1), Bim_L (SEQ ID NO: 3), Bim_{EL} (SEQ ID NO: 5) polynucleotides with human Bim_L (SEQ ID NO: 7), and Bim_{EL} (SEQ ID NO: 9) molecules. Again, these molecules are closely related isoforms of two different species. Their structure is very similar: human and mouse Bim_{EL} molecules exhibit up to 89% homology.

In conclusion, at the very least, examination of the human Bim_{EL} (SEQ ID NO: 9) and Bim_L (SEQ ID NO: 7) nucleic acid sequences is requested. Applicants further request examination of for murine Bim_S (SEQ ID NO: 1), Bim_L (SEQ ID NO: 3), Bim_{EL} (SEQ ID NO: 5) polynucleotides. An examination of five polynucleotide sequences is a reasonable number and well within the Commissioner's *sua sponte* waiver of requirements of 37 CFR §1.141 *et seq*.

Request for Withdrawal of Restriction Between Groups X and Groups VI-IX

For the reasons given above, applicants request withdrawal of the restriction between Groups VI-X, drawn to respectively to murine Bim_S (SEQ ID NO: 1), Bim_L (SEQ ID NO: 3), Bim_{EL} (SEQ ID NO: 5) and human Bim_L (SEQ ID NO: 7), and Bim_{EL} (SEQ ID NO: 9). Applicants contend that these Groups are related because they are structurally similar isoforms that are capable of being used together.

Request for Withdrawal of Restriction Between Groups V or X and Groups XI-XXII

Applicants traverse the restriction between Groups V or X and Groups XI-XXII on the grounds that Groups XI-XXII are method claims for using the novel compositions of Groups V or X and therefore under the *Ochiai* guidelines, restriction is improper.

Conclusion

Receipt of the initial Office Action on the merits is awaited. Applicants, reserve the right to file a divisional application covering the non-elected subject matter.

Respectfully submitted,

October 23, 2002
Date

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EXHIBIT 1

Sequence pair distances of Untitled ClustalW (Slow/Accurate, Gonnet)
Monday, October 21, 2002 12:50 PM

Percent Identity

Divergence

	1	2	3	4	5	6	7	
1	[redacted]	87.8	11.9	14.1	7.3	4.0	14.3	1
2	11.7	[redacted]	13.5	14.7	3.1	4.1	21.4	2
3	229.0	217.0	[redacted]	7.6	3.8	13.0	11.9	3
4	315.0	313.0	311.0	[redacted]	2.6	5.9	21.4	4
5	342.0	357.0	296.0	389.0	[redacted]	83.9	42.9	5
6	368.0	368.0	319.0	410.0	16.2	[redacted]	42.9	6
7	229.0	252.0	337.0	229.0	73.7	73.7	[redacted]	7
	1	2	3	4	5	6	7	

1 huBimEL
2 muBimEL
3 hu Bmf
4 pig r/worm cuticular collagen
5 hu Baxa
6 hu Baxb
7 hu Baxg

TABLE 1